Analyses of Susceptibility-Induced Effects on DTI Indexes in Patients with Neurodegenerative Diseases

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Introduction:

In addition to the applied diffusion-sensitizing gradients in DTI measurements, there may exist two background gradients which potentially influence diffusion measurements. First, the global background gradient which is considered uniform depends on whether it is antiparallel or parallel to the diffusion sensitizing gradient(1). Second, the local background gradient which is considered not uniform depends on the sample with intrinsic susceptibility variations such as tissues containing dispersions of iron oxide particles (2). In a diffusion MRI experiment, the magnitude of spin echoes is a function of all gradients present, and this includes a susceptibility-induced gradient in a heterogeneous sample. In addition Alzheimer's disease (AD) can be characterized pathologically by amyloid plaques, also some studies found iron accumulations in plaques in mice with AD(3,4,5), and subjects with AD had more total plaques compared with subjects MCI and normal controls (CN). (4). Therefore, in accordance with these findings, we believed that the plaques which may contain iron accumulations in AD patients may significantly cause a susceptibility-induced gradient and then alter the value of apparent diffusion coefficient (ADC), influencing diffusion tensor measurements. Moreover, the ADC obtained from the MRI experiment can be detected by Fourier transforming Stejskal-Tanner plot (6,7). The purpose of our study was to use the plots to investigate whether the ADC is contaminated in AD and MCI patients.

Methods and Materials:

Two DT-MRI sets with positive and negative polarities of diffusion sensitizing gradients were obtained in 16 AD patients, 18 mild cognitive impairment (MCI) patients, and 16 cognitive normal (CN) controls with inversion-prepared magnetization to suppress cerebrospinal fluid (CSF) on a 1.5T MRI system. DT-MRI data were acquired with a double refocusing SE single shot EPI sequence to minimize artifacts due to eddy-currents. In addition, diffusion gradients were applied in six-encoding directions with five b-values of 0, 160, 360, 640, and 1000sec/ mm^2. Mean diffusivity (MD) and fractional anisotropy (FA) maps for AD, MCI subjects were obtained for the positive (posMD and posFA), negative (negMD and neFA) diffusion gradients with home-made software. With using SPM2, the maps of FA and MD were compared between positive (posMD or posFA) and negative (negMD or neFA) polarities by performing paired T-test to find the locations of differences. We defined the regions-of-interest (ROI) based on the results of the paired T-test and obtained signal intensities from raw DT-MRI data to reveal the susceptibility-induced effects with using the positive or negative diffusion gradient.

Results:

Fig.1 displays a representative Stejskal-Tanner plot of data obtained from the ROI of the lesion in FA maps and the opposite location of the normal contra-lateral area for AD patients (p=0.0001 without adjustment for multiple comparisons). A nonlinear regression of ROI data set with using negative diffusion gradient indicates that there is an obvious curvature, but the data sets with using the positive diffusion gradient and for the opposite location of ROI almost appear linear. Additionally, Fig.2 shows that comparing the quality of ADC with ROI data from AD patients to MCI and CN subjects (p=0.0001 without adjustment for multiple comparisons), we also find that both the data sets from MCI and CN are almost linear. Similar MD maps for AD and MCI patients or FA maps for MCI patients indicate no significantly nonlinear regression in any of them, although they differ in the value of ADC.

Discussions and Conclusions:

We expected that the ADC plots showed significant nonlinear regression when using the ROI in AD to compare both FA and MD maps, but we only find an obvious curvature with using data from the FA map. According to the Fig.1 which used the data from one-direction of diffusion-encoding gradients, we find that there are obvious curvatures using the data obtained from all the six-encoding directions of ROI in AD patients for FA map. As these findings were only detected in the AD group, we hypothesize that plaques in AD patients cause the susceptibility-induced gradient and then contaminate the ADC. Therefore, we need to consider the inaccuracy of DTI measures in AD patients when obtaining DTI maps, especially for FA.

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Fig.1. The plot of roi and opposite location in AD subjects.

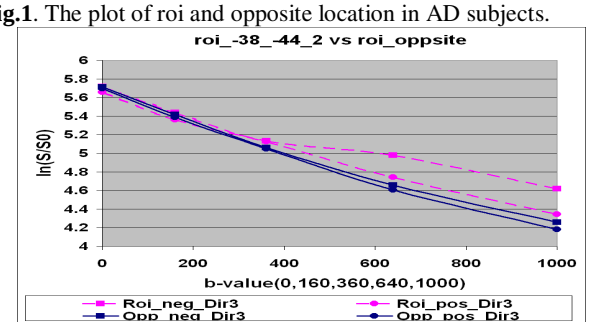

Fig.2. The plot of same ROI in AD, MCI, and CN subjects.